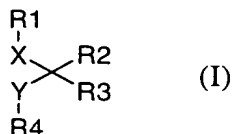


CLAIMS

1. A compound of general Formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R₁ represents,

C₁-C₆ alkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O,

and substituted with one or more basic groups such as amino, amidino and/or guanidino;

or aryl, substituted with one or more basic groups such as amino, amidino and/or guanidino,

R₂ represents H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl,

aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano,

cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z₂N-CO-O-, ZO-CO-NZ- or Z₂N-CO-NZ- group,

R₃ represents COOR₅, SO(OR₅), SO₃R₅, P=O(OR₅)₂, B(OR₅)₂, P=OR₅(OR₅), or tetrazole, or any carboxylic acid isostere,

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Sub
H1

R₄ represents a $\text{—}\overset{\text{O—R}_5}{\underset{\text{O}}{\text{P}}}\text{—R}_6$ -group, or a $\text{—}\overset{\text{O}}{\underset{\text{N—R}_7}{\text{C}}}\text{—OH}$ -group, or a $\text{—}\overset{\text{O}}{\text{C}}\text{—O—R}_5$ -group, roup,

R₅ represents H, C₁-C₆ alkyl or aryl,

R₆ represents C₁-C₆ alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted H₂N-C(Z)-CONH-C(Z)- or H₂N-C(Z)- group,

R₇ represents H or C₁-C₆ alkyl,

X represents O, S, SO, SO₂, C(Z)₂, N(Z), NR₇SO₂, SO₂NR₇, NR₇CO or CONR₇,

Y represents O, N(Z), S, C(Z)₂, or a single bond,

Z represents independently H, C₁-C₆ alkyl, aryl, cycloalkyl or heterocyclyl, with the proviso that when X represents O, S, SO, SO₂, N(Z), NR₇SO₂, SO₂NR₇, or NR₇CO then Y represents C(Z)₂ or a single bond.

2. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R₁ represents,

cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O, and substituted

with one or more basic groups such as amino, amidino and/or guanidino;

R₂ represents H, C₁-C₃ alkyl, amino, halogen, hydroxy,

R₃ represents COOR₅,

R₄ represents a $\text{—}\overset{\text{O—R}_5}{\underset{\text{O}}{\text{P}}}\text{—R}_6$ -group,

R₅ represents H, C₁-C₆ alkyl or aryl,

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R₆ represents C₁-C₆ alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted
H₂N-C(Z)-CONH-C(Z)- or H₂N-C(Z)- group,

X represents C(Z)₂,

Y represents O or C(Z)₂,

5 Z represents independently H or C₁-C₆ alkyl.

3. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

10 R₁ represents,

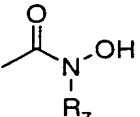
cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

15 heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R₂ represents H, C₁-C₃ alkyl, amino, halogen or hydroxy,

R₃ represents COOR₅,

R₄ represents a  -group,

R₅ represents H, C₁-C₆ alkyl or aryl,

20 R₇ represents H or C₁-C₆ alkyl,

X represents C(Z)₂,

Y represents C(Z)₂, or a single bond,

Z represents independently H or C₁-C₆ alkyl.

25 4. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R₁ represents,

cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

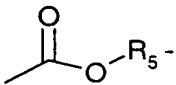
heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O,

5 and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R₂ represents H, C₁-C₃ alkyl, amino, halogen or hydroxy,

R₃ represents COOR₅,

10 R₄ represents a -group,

R₅ represents H, C₁-C₆ alkyl or aryl,

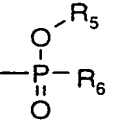
X represents C(Z)₂,

Y represents C(Z)₂, or a single bond,

Z represents independently H or C₁-C₆ alkyl.

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5. A process for the preparation of a compound according to any one of claims 1-4, wherein R₁, R₅, R₆, and Z are as defined in claim 1 and R₂ is H, R₃ is COOR₅,

R₄ represents a -group,

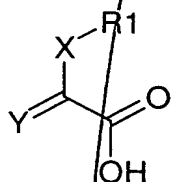
X is C(Z)₂, Y is C(Z)₂,

comprising the step of:

20 reacting a compound of Formula VI,

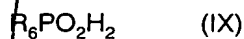
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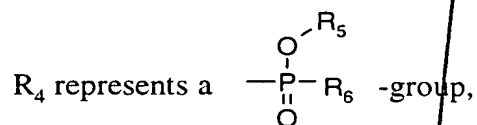
(VI)

wherein R_1 and Z is as defined in claim 1 and X is $\text{C}(\text{Z})_2$ and Y is $\text{C}(\text{Z})_2$ with a compound of Formula IX,



wherein R_6 is as defined in claim 1, in the presence of a suitable reagent, such as BSA or HMDS, under standard conditions.

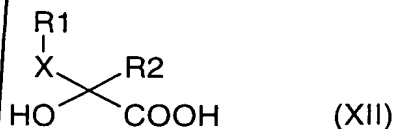
6. A process for the preparation of a compound according to any one of claims 1-4, wherein R_1 , R_2 , R_5 , R_6 , and Z are as defined in claim 1, R_3 is COOR_5 , X is $\text{C}(\text{Z})_2$, Y is O ,



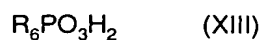
and

comprising the step of:

reacting a compound of Formula XII,



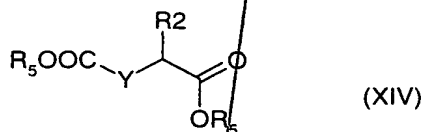
wherein R_1 and R_2 are as defined in claim 1 and X is $\text{C}(\text{Z})_2$ with a compound of Formula XIII,



wherein R_6 is as defined in claim 1, in the presence of suitable coupling reagents such as DCC/DMAP, PyBop/DIPEA or SOCl_2 , under standard conditions.

7. A process for the preparation of a compound according to any one of claims 1-4,

wherein R_1 and R_2 are as defined in claim 1 and X and Y is $\text{C}(\text{Z})_2$ or a single bond and R_3 and R_4 are COOR_5 , comprising the step of:
reacting a compound of Formula XIV,

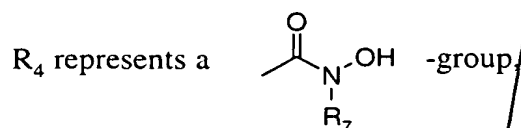


wherein R_2 and R_5 are as defined in claim 1 and Y is $\text{C}(\text{Z})_2$ or a single bond, with a compound of the general Formula III,



wherein R_1 is as defined in claim 1, X is $\text{C}(\text{Z})_2$ and L is a suitable leaving group, such as Cl, Br, I or tosyl, in the presence of a suitable base, such as LDA or NaH, under standard conditions.

8. A process for the preparation of a compound according to any one of claims 1-4, wherein R_1 , R_2 , R_5 , R_7 , X, Y and Z are as defined in claim 1, R_3 is COOR_5 and



comprising the step of:
reacting a compound of Formula XV,

- (i) a compound of Formula I or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, and
- (ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P₂T) antagonist,
- in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

15. A kit of parts comprising:

- (i) a pharmaceutical formulation containing a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- (ii) a pharmaceutical formulation containing one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P₂T) antagonist, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier;
- which compound (i) and agent (ii) are each provided in a form that is suitable for administration in conjunction with the other.

16. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a therapeutically effective total amount of

- (i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; in conjunction with
- (ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P₂T) antagonist,

in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

17. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation as defined in claim 15.

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